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THE AUDITORY BRAINSTEM RESPONSE (ABR) IS A USEFUL DIAGNOSTIC TOOL IN THE INTENSIVE CARE NURSERY

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SUMMARY

We present normative data on the auditory brainstem response (ABR) derived from 91 premature infants, and illustrate a simple procedure that uses deviations from these norms to differentiate a hearing disorder from a neurological disorder involving the brainstem. In an infant intensive care unit the procedure identified 11 patients with hearing disorder, 3 with neurological problems, and 3 with both disorders. Serial measurements revealed whether a given infant was developing normally, and, for those with disorders, whether the clinical status was improving or deteriorating. The ABR method, which is non-invasive and performed during natural sleep, provided useful diagnostic information about every infant tested.

SPECULATION

The hard, objective data this new method provides adds a potentially important tool to the neurological armamentarium. Additional research will reveal whether, as we suggest here, its use accurately predicts where and how much brain and cochlear damage is produced by anoxia, acidosis, trauma, drug regimes and the like, and establish its value as a method for monitoring clinical status - unchanged improving, deteriorating, brain death.

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Scalp electrodes permit visualization of electrical events generated in brainstem structures. The method readily identifies newborns with hearing loss, brainstem neurological involvement, or both.

INTRODUCTION

The auditory brainstem response (the ABR: 7,14) is proving to be increasingly useful in the diagnosis of adult and infant disorders (9,10,13,16,17,18, 20,22). It yields unequivocal information on the threshold sensitivity of the peripheral auditory apparatus (cochlea and auditory nerve) and in addition it accurately estimates the velocity of conduction in the auditory fibers ascending through the brainstem enroute to the cortex. It thus provides, directly and simply, precise neurophysiological data to aid both otological and neurological diagnoses.

The infant ABR consists of three major waves (I, III, V) evoked by an auditory stimulus such as a click; it is extracted from the scalp-recorded EEG by computer techniques. Wave I is generated by the auditory nerve action potentials while wave V originates in neural activity in the region of the inferior colliculus. The entire phenomenon lasts about 10 msec.

Several authors (5,6,8,11,12,15,19) have studied the ABR in normal infants. The phenomenon appears at around 26 wks gestational age and thereafter undergoes systematic changes in latency (a shortening), amplitude (an increase) and threshold (a drop). At around one year of age the maturation of the cochlea and brainstem pathways has apparently been completed, for the ABR at that age closely resembles that of an adult.

An example of the changes under discussion is to be seen in Fig. 1, a series of responses obtained from a premature infant. It shows the ABR waves to shorten in latency 1) as the infant matures week-by-week and 2) as the sound intensity increases. Also evident are 3) an age-dependent drop in the minimal stimulus intensity necessary to produce the response and 4) an increase in response amplitudes. Both the threshold stimulus required and the way wave V latency shortens with intensity provide the information of otological interest (3,4,22). The neurological information, on the other hand, is derived from measurement of the latency and amplitude of each of the ABR waves (17); the interval between waves I and V is of particular diagnostic value for it measures the time taken for impulses to travel within the brainstem to the inferior colliculus level.

In this paper we report ABR measurements made on infant patients in an intensive care unit. We first describe data obtained from those considered to be essentially free of audiological and neurological disorders, and then deal with the pathological ABRs found in 17 cases.

METHODS

Of the 108 subjects in this series 100 represented 97% of the infants in the intensive care nursery at the Children's Hospital, San Diego, during a 5-month period in 1977. The remaining 8 were referred later by neonatologists. With one exception the babies varied between 26 and 42 wks estimated ga at test. Most were undergoing perfusions, on aided respiration and being monitored for cardiac function at the time. More than 70% were receiving or had received one or more ototoxic drug. Usually both ears were tested; an occasional normal infant was tested only monaurally.

Testing took place in isolettes or open basinettes. Standard disc electrodes were attached to the vertex and both mastoids by standard techniques, as explained elsewhere (12). Interelectrode impedances were all below 8000 ohms. Stimuli generated by 0.1 msec square waves were delivered monaurally, after attenuation, to a TDH-39 earphone taped over the infant's ear. Zero dB was established as the mean threshold for 6 adults with normal audiograms listening to the clicks in a quiet room. Recordings consisted of the average of 2000 amplified responses, vertex positive up, made with a Nicolet CA 1000 averager with its amplified bandpass set at 150-1500 Hz. Testing on most babies was completed (both ears) within an hour.

The procedure began with an attempt to obtain an ABR to clicks at 60 or 70 dB, after which an intensity series like those in Fig. 1 was obtained. The initial click rate was usually 37 per sec., but rates between 10 and 80 per sec were also used (usually at the 60 dB level) with most suspected pathological cases and many normals. The procedure used to detect and classify abnormal responses is described in detail in a later section.

RESULTS

Normative Data

1. Latency-Intensity Functions

Figure 2 shows the wave V latency values obtained at various gestational ages from those infants in our sample (N=91, 135 ears) presumed to be neurologically and audiologically normal. A "normal" infant is one who yielded apparently normal ABRs to the 60 dB click at the time of test and to the 30 dB click either at that time or (for the very young ones) at a test some weeks later. This figure, derived from intensity series' like those shown in Figure 1, demonstrates the three factors known to influence wave V latency; the latency shortens with age (by approximately 0.2 msec per week through this period), with stimulus intensity increase (by about 30 microsecs per dB) and with decrease in stimulus rate. The influence of stimulus rate is more fully treated in the next section.

The dotted curves in Fig. 2 come from previously published studies reporting on these same phenomena. The remarkable agreement between these data and that reported here indicates that the maturation of the neural substrate for the ABR proceeds in essentially the same way in all premature babies. The rules by which these maturational processes proceed appear therefore to be stable and highly reliable, thus making the ABR a dependable diagnostic tool.

In our series 42 infants were tested at 34 wks ga; of these 16 were a few days old at the time of test while 26 had been born 1 to 5 weeks earlier. The wave V latencies of the 26 born previously overlapped (at both the 60 and 30 dB values) with those of the newly born, indicating that the maturation of the system tested by ABR proceeds at the same rate whether the infant has been in or out of the uterus. This conclusion confirms a similar finding reported by Starr et al. (19).

Figure 3 adds the latencies of wave I to those of wave V for the sample. Evidently most of the wave V latency change prior to about 34 wks ga. is due to cochlear maturation since its shortening in this period (1.1 msec) approximates that of wave I (.95 msec). Between 35 and 40 weeks, however, the decrease in wave V latency outstrips that of wave I by a factor of about 3, indicating that the more important changes occurring in this period are taking place within the brainstem. Presumably myelination and/or increased synaptic efficiency is responsible for this decrease in the conduction time between the auditory nerve level (wave I) and the inferior colliculus (wave V).

2. Rate Effects

The effect of stimulus rate upon the ABR has been examined in adults (1, 10). The rationale for such studies is the possibility that in the presence of disease the auditory brainstem pathways might fail to conduct impulses properly when driven at high stimulus rates. To provide some normal baseline data for premature infants we examined the effects of stimulus rate in 18 of them. Figure 4 shows the wave V latencies noted at rates between 10 and 80 per sec for one adult and for a few of the babies in the sample. The failure of wave V to appear at rates above 40 per sec in the baby 30 wks old suggests that the auditory pathway at that age is still insufficiently developed to transmit impulses at high rates. From 32 weeks onward, however, wave V responses were uniformly obtained at rates as high as 80 per sec. Furthermore, the slopes of these rate curves (in microseconds for each 10 per sec change in rate) steadily declined from about 270 (30 wks) through 190 (32 wks) and 110 (40 wks) toward the adult value of 35 or 40. This indicates that with maturation in this period of life the brainstem pathways become increasingly competent in their ability to follow high rates of stimulation.

Figure 5 summarizes the rate data for 16 of the babies in this group. The wave V latencies measured for a given subject at 10 and 80 per sec are connected by a vertical line in the upper part of the figure; in each case the latency is about 1 msec longer at 80 as compared to 10 per sec. In the lower part the I-V intervals at the two rates are similarly connected; the rate-dependent increase is around 0.5 msec. The figure further separates the infants into 2 groups on the basis of age; the horizontal lines give the means of the values obtained at the indicated rate in each group. Values expected at rates between these extremes can be estimated by linear extrapolation.

These rate studies permit two major conclusions. First, the brainstem auditory pathways will conduct impulses at rates as high as 80 per sec (interstimulus interval 12.5 msec) in normal infants from about 32 wks onward. Second, since the rate-dependent increase in the latency of wave V is approximately twice that of wave I, about half of the rate effects seem to occur at the cochlear level and half in the brainstem conduction time.

The main reason for assembling this normative information on the influence of stimulus rate was to permit comparisons with similar measurements made on patients with neurological disorders. Our sample of neurological patients on whom this potential diagnostic tool was tested is small but, as Fig. 9 shows, it did on occasion prove useful.

Abnormal ABRs

1. Diagnostic Criteria

ABR information is currently being used, as stated in the Introduction, to aid both audiological and neurological diagnoses. The audiological information is derived from two measurements made on wave V: threshold sensitivity is estimated by establishing the weakest stimulus that produces wave V, and the type of hearing loss (conductive, sensorineural) can often be identified from a graph showing the manner in which wave V latency shortens as intensity increases (4,8,9,13,22).

As established in the previous section a given premature infant can be considered audiologically abnormal if he fails to meet three criteria: 1) an ABR response to the 30 dB click at age 35 wks and older; 2) a wave V latency to the 60 dB click that falls within the range shown for this age group (Fig. 2); and 3) a slope of the wave V latency vs intensity curve (derived from intensity series recordings like those of Fig. 1) of between 30 and 40 microseconds per dB of intensity change. Similarly, he can be considered neurologically abnormal if his ABR shows the features widely accepted as indicating neurological disorder in adults: 1) an abnormally prolonged I-V interval, 2) amplitude abnormality of one or more of the component waves, and 3) a mixture of the above (10,17,18,20,21).

Using these criteria we have devised a procedure that identifies the normal baby and separates the ones with audiological abnormality from those with neurological abnormality. This procedure involves the series of steps illustrated in Fig. 6. The first step is an attempt to obtain the ABR to a 60 or 70 dB click at a rate between 10 and 70 per sec. Absence of response to such a stimulus at any age signifies severe audiological disorder which requires further investigation using stimulus intensities up to equipment limits. Presence of a response calls for measurement of its wave V latency and comparison of this value with the norms for age (Fig. 2); if wave V is prolonged, the I-V interval must also be measured (Fig. 3). These measurements make possible several diagnostic statements. First, if wave V is normal for age and intensity the I-V interval will also be normal, and so neurological disorder is unlikely. Second, if wave V is prolonged but the I-V interval is normal, a hearing loss is indicated. Third, if the I-V interval is prolonged with wave I normal for age, a neurological disorder is probable. Finally, if both I and the I-V interval are prolonged, neurological and audiological disorders are both suggested.

After these measurements on waves I and V have been made another ABR is sought using the 30 dB click. A response to this 30 dB signal virtually assures that the infant is audiologically normal; if no ABR is obtained the stimulus intensity is to be increased until the response threshold is established, after which the wave V latencies to suprathreshold stimuli are obtained and charted.

2. Patients with ABR Abnormality

Seventeen infants failed to meet the ABR criteria for normal audiological and/or neurological status. The abnormalities noted are illustrated in Figs. 6 through 9. On the basis on these the patients can be divided into 4 groups.

Group I (N=3). No ABR appeared to the 90 dB click applied to either ear. All these babies had suffered severe asphyxia at birth and one in addition exhibited a congenital craniofacial malformation (cleft palate). In cases such as these one can conclude that the infant is deaf to signals up the strength of the one employed, but since no ABR is available for analysis, the method sheds no light upon the infant's neurological status.

Group II (N=1). Only wave I appeared, and this to the 90 and 80 dB signals alone. According to the diagnostic criteria both audiological disorder (greatly elevated threshold) and neurological disorders (failure of conduction through the brainstem pathways) existed in this patient.

Group III (N=5). The I-V interval was prolonged (4 cases) and/or the amplitudes of the ABR components were abnormal, particularly at high rates of stimulation. In addition, a threshold elevation was present in 2 cases. Patients in this group are considered to suffer predominantly neurological disorders. Their clinical histories all suggested depression of brainstem function following brain hemorrhage, intracerebral hematoma or prolonged seizures following a period of severe asphyxia. Following treatment several of these patients gave normal or near normal ABRs. Case histories of two of them are given below.

Group IV (N=8). The I-V interval fell within the normal range for age, but wave V was prolonged to the 60 dB click and the click threshold was elevated (see Fig. 6 for an illustration). These infants are considered to suffer hearing loss without additional neurological disorder. We reserve further discussion of this group for a comparion report (2) in which we present a detailed analysis of their clinical histories in an attempt to identify the factors responsible for their hearing losses.

3. Case Histories

Case 1. Baby T, one of a pair of identical female twins born at an estimated 26 wks ga, required assisted ventilation and suffered an intraventricular hemorrhage followed by a period during which the EEG was flat during her first 3 postpartum weeks. Baby L, her sister, underwent an operation to correct a patent ductus arteriosis during this same period but otherwise thrived. ABR responses were obtained from each baby at approximately weekly intervals during their hospital stay. The I-V intervals extracted from these records are shown in Fig. 7 plotted as a function of gestational age. A prolongation of 1 msec or so is evident in baby T's recordings compared to those of her sister until about their 35th week, after which the I-V intervals in their recordings shorten similarly. We interpret these results as showing that the ABR can provide a useful measure of the recovery of function in a brainstem presumably damaged by some intracranial mechanical or metabolic disorder secondary to the intracranial hemorrhage. The gradual resolution of this disorder is indexed by shortening of the I-V interval until it attains the normal value at around week 35.

Case 2, a full term baby born at home, was brought to the hospital several hours later severely asphyxiated and acidotic. Prolonged seizures and deep coma with absent reflexes preceeded his death at 3 days. Sample ABRs taken during this period are illustrated in Fig. 8. These show a greatly reduced wave V amplitude and a near-normal I-V interval. The amplitude abnormality of wave V was most prominent at high stimulus rates. No ABR could be obtained below 55 dB and so both a sensorineural hearing loss and dysfunction of the upper brainstem can be inferred from the recordings.

DISCUSSION AND CONCLUSIONS

We report here normative ABR data obtained from a group (N=91) of premature infants in an intensive care nursery. The babies are presumed to have normal hearing and no neurological disease. The ABR was invariably obtained at 28 wks ga. and beyond. Furthermore, systemmatic age related changes in the amplitudes and latencies of the component waves took place, and the threshold of the response dropped. Evidently the anatomical and physiological basis for the ABR phenomena are common to all babies and the response itself precisely mirrors the continued maturation of the cochlea and the brainstem auditory pathways taking place during this period of life.

We also report and illustrate a method for using the ABR as a diagnostic tool to differentiate a hearing disorder from a neurological disorder involving the brainstem. For the normal infant 2 recordings from each ear can virtually exclude the possibility of either disorder; each record requires about 5 minutes to obtain.

The method identified 17 infants with ABR abnormalities who were then separated into 4 groups. One group yielded no response whatever, and so was deaf to the stimulus used. Another showed evidence of cochlear function but no activity in the brainstem pathways. A third yielded ABRs with altered latencies and/or wave shapes interpreted as due to impaired brainstem function. The final group was neurologically normal but showed various amounts of hearing loss.

The test was serially applied to a number of patients at daily or weekly intervals in an attempt to assess the amount of brainstem involvement accompanying their disease. In 2 cases of intraventricular hemorrhage the ABR abnormality receded or disappeared as clinical status improved. ABR monitoring in infancy may, therefore, prove as useful a method for evaluating day-by-day alterations in brainstem function as it is in adults.

In our experience the ABR proved to be an acceptable and informative procedure in the intensive care unit. It is acceptable to the nursing staff because, being non-invasive, it does not disturb or irritate the babies. The information it provides to the neonatologist has often been of considerable value. ABR changes sometimes precede - and so predict-clinical improvement or deteriorations, and the next step in the management of very sick babies has sometimes turned on the question of whether its ABR was normal or not. The ability of the ABR to pin-point the auditory threshold so readily has, finally, enabled the pediatrician for the first time to make an unequivocal diagnosis about hearing level.

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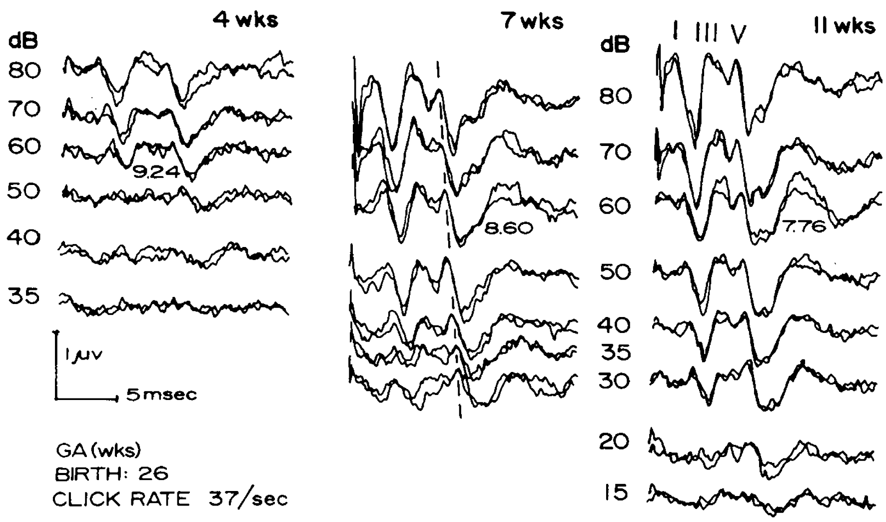

Fig. 1. Maturation of the auditory brainstem response in a premature infant born at 26 weeks gestational age. The prominent vertex positive waves seen in most recordings are labelled (I, III, V) in the 11 weeks (37 wks ga.) record to 80 dB clicks. The numbers beneath the 60 dB records give the latency of wave V in msec. In the intensity series made at 7 wks (33 wks ga.) a dashed line connects the waves V. This figure illustrates the way response components increase in amplitude and decrease in latency as both age and stimulus intensity increase, as well as the drop in threshold accompanying maturation.

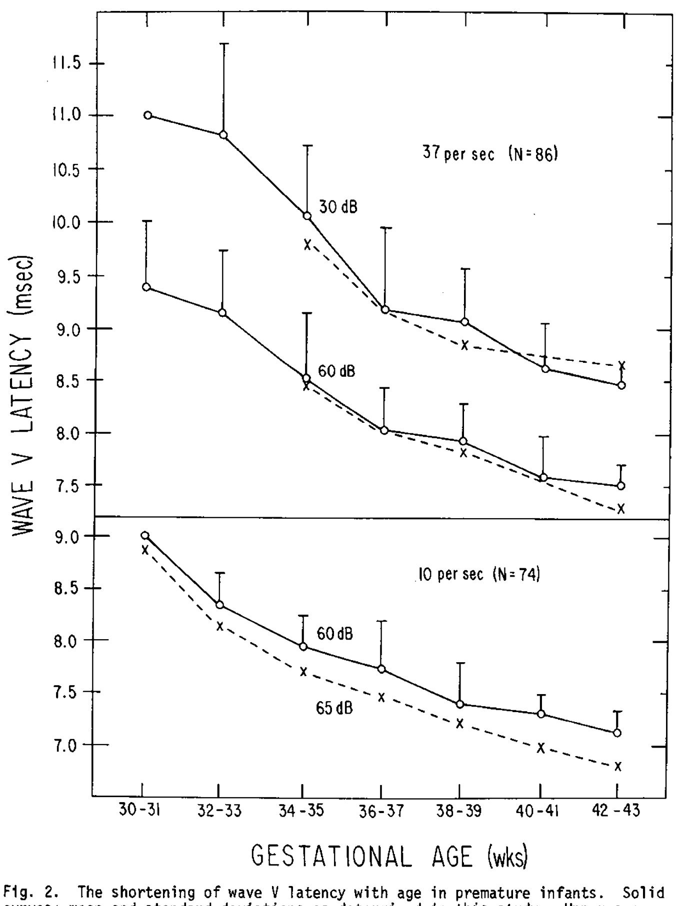

Fig. 2. The shortening of wave V latency with age in premature infants. Solid curves: mean and standard deviations as determined in this study. Upper section, with click stimulus rate at 37 per sec., lower section, 10 per sec rate. Stimulus intensity is indicated next to each curve. The dotted curves in the upper section replot the data of (12), those in the lower section that of (19).

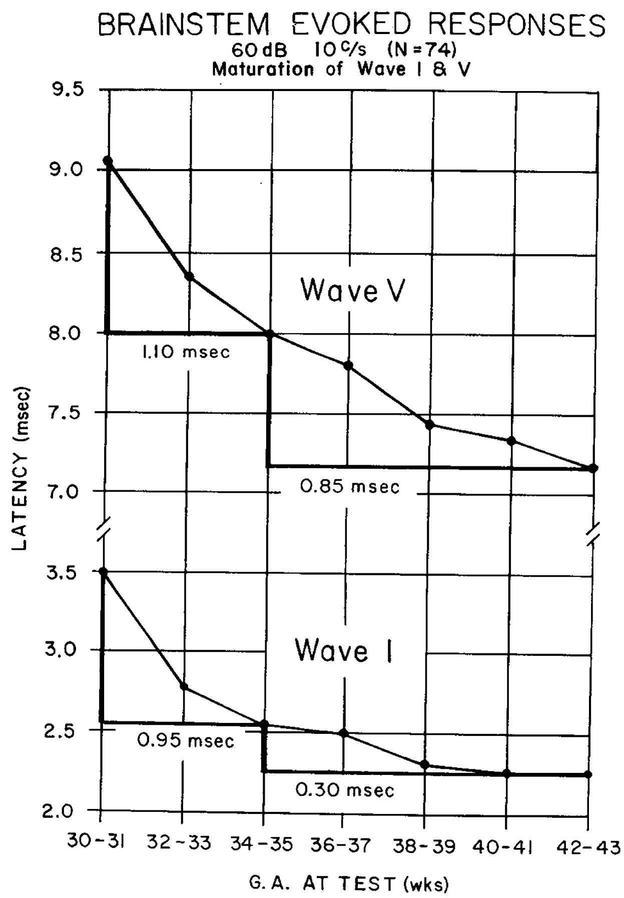

Fig. 3. Decrease in the latencies of waves I and V with age in prematures. Test stimulus 60 dB, 10 per sec clicks.

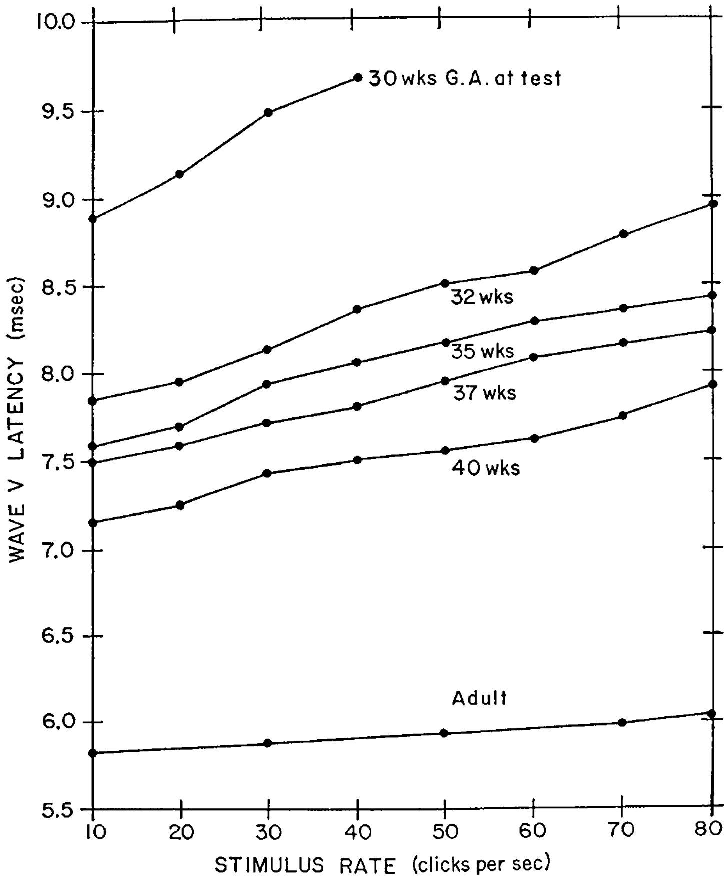

Fig. 4. Effect of stimulus rate on wave V latency for 5 infants and 1 adult. Monaural clicks, 60 dB.

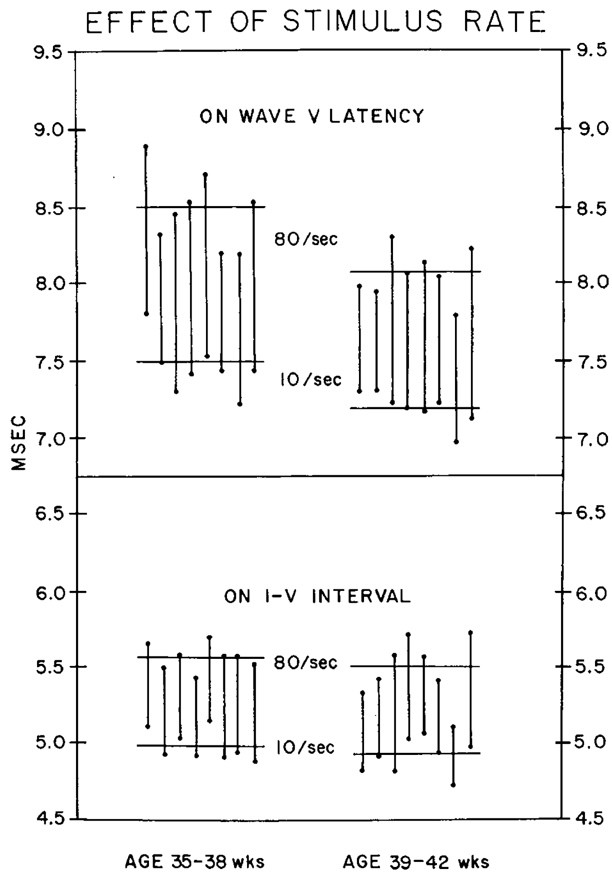

Fig. 5. The effect of stimulus rate on wave V latency (upper chart) and on the I-V interval (lower chart) for 16 babies of different age. Each vertical line connects the values obtained for one baby at the 80 and 10 per sec rates. Horizontal lines represent the mean values for each group and rate. Monaural clicks, 60 dB. Data obtained from plots of waves V and I like those in Fig. 4.

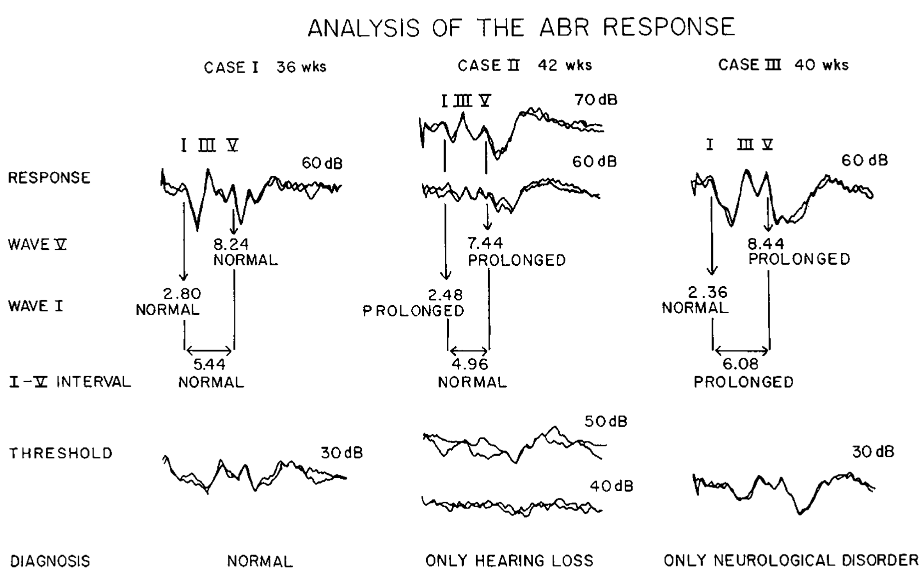

Fig. 6. Step-by-step procedure for analyzing ABR recordings (left column) applied to 3 cases.

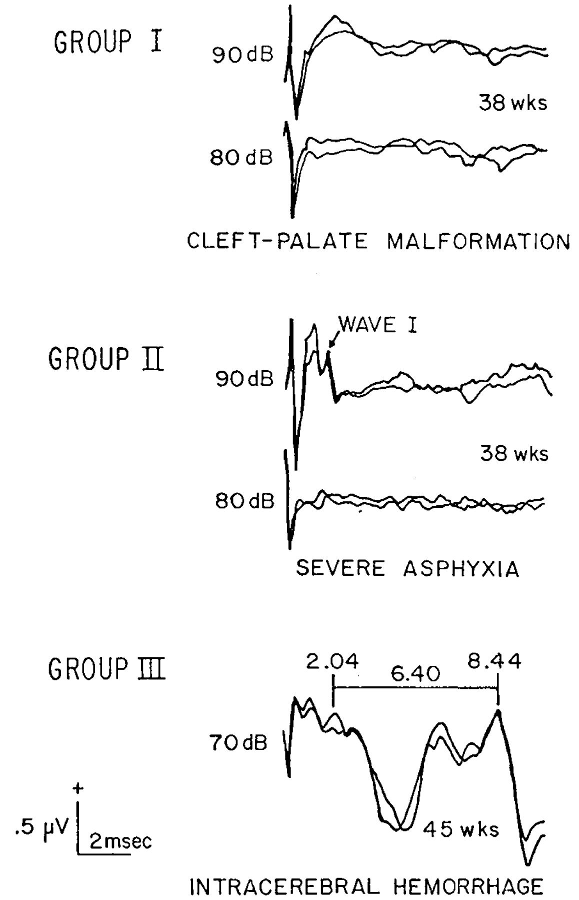

Fig. 7. Typical abnormalities encountered in premature patients. Group 1: no response obtained with clicks of highest available intensity; patient has severe hearing loss. Group 2; only wave I appears; cochlea functions but brainstem pathways fail to conduct impulses. Group 3: the interval between waves I and V is prolonged; brainstem function is depressed with consequent increase in brainstem conduction time.

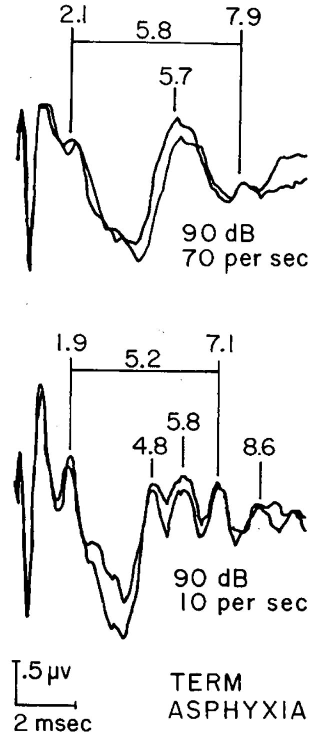

Fig. 9. Abnormal ABRs from a severely asphyxiated term newborn showing near-normal cochlear function (wave I latency about 2 msec); impaired brainstem function is indicated by reduced wave V amplitudes and abnormal waveshapes most evident at the high stimulus rate.

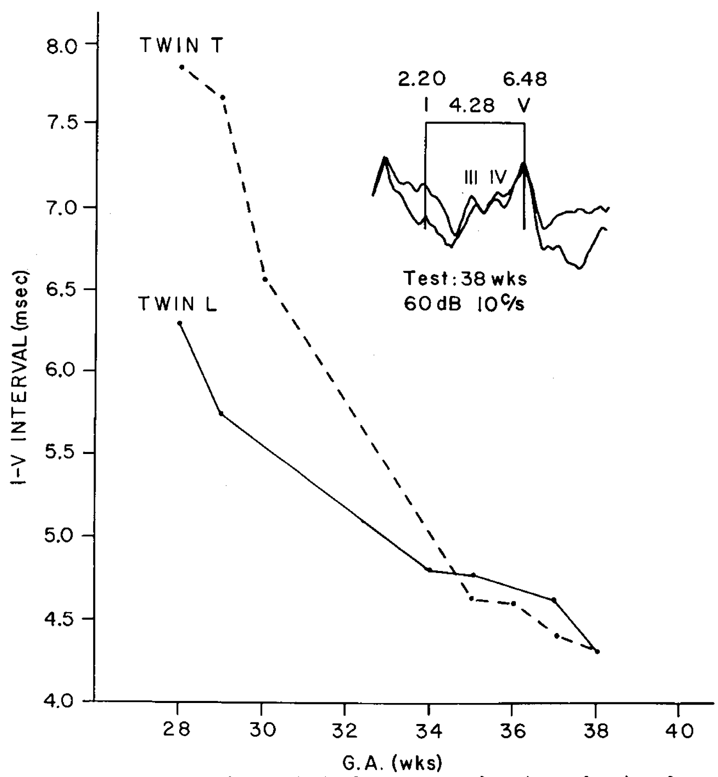

Fig. 8. The I-V intervals of twin female prematures plotted as a function of their age. Twin T suffered an intracranial hemorrhage at around 26 wks; the elevated I-V interval until age 35 wks is presumably due to depressed brainstem function secondary to the hemorrhagic episode.

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